STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 175065

TO: Rei-Tsang Shiao
Location: rem/5A10/5C18
Art Unit: 1626
Tuesday, January 10, 2006
Case Serial Number: 10/757098

From: Barb O'Bryen
Location: Biotech-Chem Library
Remsen 1a69
Phone: 571-272-2518

barbara.obryen@uspto.gov

Search Notes

ACCESS DB # 175065

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Scientific and Technical Information Center

SEARCH REQUEST FORM

Requester's Full Name: Robert (Reiko) Shiao Examiner #: 79521 Date: 12/27/05

Art Unit: 1626 Phone Number: 2-0707 Serial Number: 10/757,098

Location (Bldg/Room#): KEM (Mailbox #): 5A/96 Results Format Preferred (circle): PAPER DISK

****

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:

Title of Invention: phospholipid deriv of non-steroid MEI

Inventors (please provide full names): Kaszk et al

Earliest Priority Date:

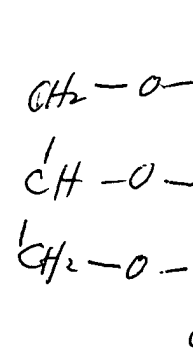
Search Topic:

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known.

RECEIVED DEC 27 2005 (STIC) CHEM/BIOTECH DIVISION

For Sequence Searches Only *Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

I. Search cpd I (see claim 1)



10. * R^1, [illegible] see sub
* R^2 is choline, ethanolamine, inositol, serine.
* Z is C
* X is N, S, C
* D is ibuprofen (see attachment)

II. methods of use of cpd I

IN THE CLAIMS

Please cancel claims 8, 18, 27 and 33 without prejudice.

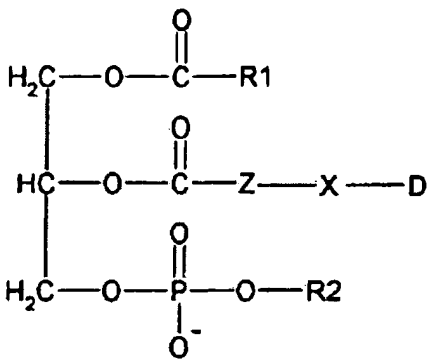
Please amend claims 1, 10, 11, 20 and 30 as indicated below.

Please withdraw claims 28-32 from consideration herein.

The listing of claims below will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently Amended) A compound of the general formula I



Formula I

or a pharmaceutically acceptable salt thereof, wherein:

R1 is a saturated or unsaturated~~, substituted or unsubstituted~~ hydrocarbon chain having from 2 to 30 carbon atoms;

R2 is ~~H or~~ a phospholipid head group;

D is ~~the residue of a nonsteroidal anti-inflammatory drug having a functional group selected from the group consisting of carboxyl, hydroxyl, amine and thiol~~ ibuprofen, wherein D is attached through ~~said~~ a functional group to a bridging group, -C(O)-Z-X- , wherein Z is a saturated or unsaturated hydrocarbon chain having from 2 to 15 carbon atoms, and X is ~~selected from~~ an amino~~, hydroxy, thio and carbonyl groups, such that when the functional group of D is~~

~~carboxyl, X is selected from amino, hydroxy and thio, and when the functional group of D is amino, hydroxy or thio, X is a carbonyl~~ group.

2. (Previously Presented) The compound according to claim 1, wherein the conjugated residue of the nonsteroidal anti-inflammatory drug is pharmacologically inactive.

3. (Original) The compound according to claim 1, wherein an ester bond at position sn-2 of the phospholipid of the general formula I is cleaveable by a lipase.

4. (Original) The compound according to claim 3, wherein said lipase is a phospholipase.

5. (Original) The compound according to claim 4, wherein said phospholipase is phospholipase A_2 (PLA_2).

6. (Original) The compound according to claim 1, wherein R1 is an hydrocarbon chain having from 10 to 20 carbon atoms.

7. (Original) The compound according to claim 1, wherein R1 is an hydrocarbon chain having 15 or 17 carbon atoms.

8. (Canceled)

9. (Original) The compound according to claim 1, wherein R2 is selected from the group consisting of choline, ethanolamine, inositol and serine.

10. (Previously Presented) The compound according to claim 1 selected from the group consisting of:

~~1-Stearoyl-2-{3-[2-(2,6-dichloroanilino)phenylacetamido]propanoyl}-sn-glycero-3-phosphocholine,~~

~~1-Stearoyl-2-{4-[2-(2,6-dichloroanilino)phenylacetamido]butanoyl}-sn-glycero-3-phosphocholine,~~

~~1-Stearoyl-2-{5-[2-(2,6-dichloroanilino)phenylacetamido]valeroyl}-sn-glycero-3-phosphocholine,~~

~~1-Stearoyl-2-{6-[2-(2,6-dichloroanilino)phenylacetamido]hexanoyl}-sn-glycero-3-phosphocholine,~~

~~1-Stearoyl-2-{8-[2-(2,6-dichloroanilino)phenylacetamido]octanoyl}-sn-glycero-3-phosphocholine,~~

~~1-Stearoyl-2-{12-[2-(2,6-dichloroanilino)phenylacetamido]dodecanoyl}-sn-glycero-3-phosphocholine,~~

~~1-Stearoyl-2-{3-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl indolylacetamido]propanoyl}-sn-glycero-3-phosphocholine,~~

~~1-Stearoyl-2-{4-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl indolylacetamido]butanoyl}-sn-glycero-3-phosphocholine,~~

~~1-Stearoyl-2-{5-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl indolylacetamido]valeroyl}-sn-glycero-3-phosphocholine,~~

~~1-Stearoyl-2-{6-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl indolylacetamido]hexanoyl}-sn-glycero-3-phosphocholine,~~

~~1-Stearoyl-2-{8-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl indolylacetamido]octanoyl}-sn-glycero-3-phosphocholine,~~

1-Stearoyl-2-{3-[α-methyl-4-(2-methylpropyl)benzeneacetamido] propanoyl}-sn-glycero-3-phosphocholine, and

1-Stearoyl-2-{6-[α-methyl-4-(2-methylpropyl)benzeneacetamido] hexanoyl}-sn-glycero-3-phosphocholine~~,~~

~~1-Stearoyl-2-{3-[(S)-6-methoxy-α-methyl-2-naphtaleneacetamido]-propanoyl}-sn-glycero-3-phosphocholine,~~

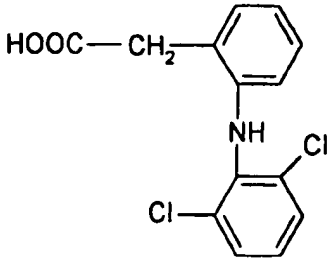
~~1-Stearoyl-2-{4-[(S)-6-methoxy-α-methyl-2-naphtaleneacetamido]-butanoyl}-sn-glycero-3-phosphocholine,~~

~~1-Stearoyl-2-{6-[(S)-6-methoxy-α-methyl-2-naphtaleneacetamido]-hexanoyl}-sn-glycero-3-phosphocholine, and~~

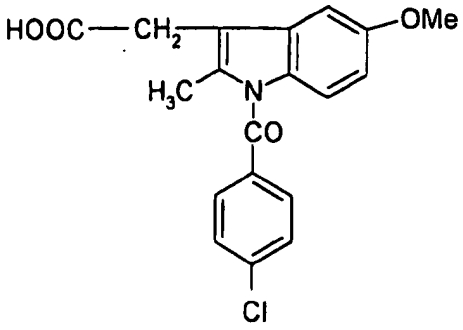
~~1-Stearoyl-2-{4-[2-(6-methoxynaphtyl)acetamido]butanoyl}-sn-glycero-3-phosphocholine~~.

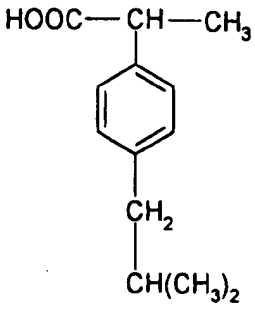
Wherein HOOC-R_d in the synthesis scheme is a non-steroidal anti-inflammatory drug. For example, HOOC-R_d may be selected from:

Diclofenac

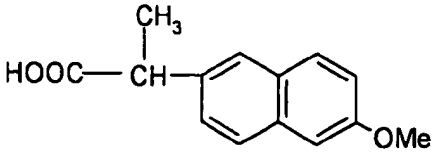


Indomethacin

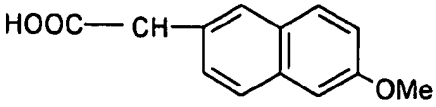




Ibuprofen



Naproxen



6-Methoxy-2-naphthylacetic acid

Chemical analysis: $C_{53}H_{83}N_3O_{11}PCl \cdot 2H_2O$.

Calculated: C 61.16%, H 8.46%, N 4.09%, P 3.03%, Cl 3.41%.

Found: C 61.21%, H 8.37%, N 4.04%, P 2.98%, Cl 3.47%.

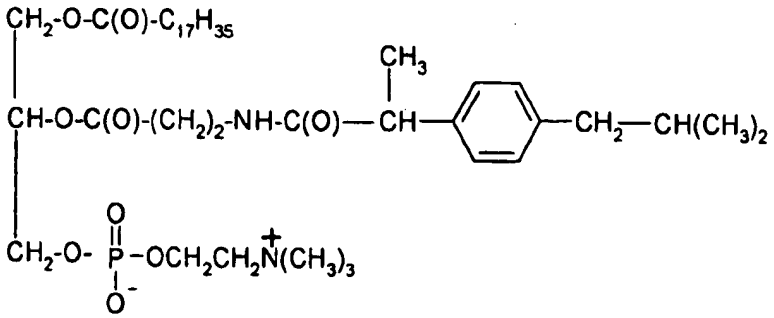
EXAMPLE 3: Preparation of lipid derivatives of ibuprofen (DP-Ibu)

The procedure for the preparation of lipid derivatives of ibuprofen (2-(4-isobutylphenyl)propionic acid) is the same as the process outlined in Example 1, steps 1 to 6, except that in step 6 instead of diclofenac the drug included in the reaction mixture is ibuprofen.

Lipid derivatives of ibuprofen (DP-Ibu)

The synthesized compounds were subjected to TLC analysis under the following conditions: Silica gel 60 on aluminum sheet. Eluent is chloroform:methanol:water (65:35:5, v/v). Indicator is a spray of the composition: 4-methoxybenzaldehyde (10 ml), absolute ethanol (200 ml), 98% sulfuric acid (10 ml) and glacial acetic acid (2 ml). The chromatogram is sprayed with the indicator and then charred at 100°C.

1-Stearoyl-2-{3-[α-methyl-4-(2-methylpropyl)benzeneacetamido]propanoyl}-sn-glycero-3-phosphatidylcholine.



White wax. Hygroscopic. Yield 60%.

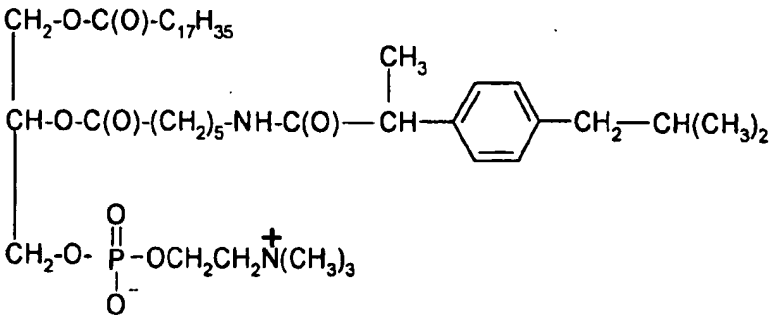
TLC analysis: One spot. R_f is 0.38.

^{1}H NMR (CD_3OD), δ (ppm): 0.88-0.93 (m, 9H), 1.29 (s, 28H), 1.41-1.44 (d, 3H), 1.58-1.63 (m, 2H), 1.80-1.90 (m, 1H), 2.28-2.35 (t, 2H), 2.43-2.46 (d, 2H), 2.51-2.57 (t, 2H), 3.22 (s, 9H), 3.40-3.45 (m, 2H), 3.61-3.66 (m, 3H), 3.98-4.41 (several m, 6H), 5.18 (m, 1H), 7.01-7.07 (d, 2H), 7.22-7.26 (d, 2H).

^{31}P NMR (CD_3OD), δ (ppm): -0.20(s).

Chemical analysis: $C_{42}H_{75}N_2O_9P$. $4H_2O$. Calculated: C 59.02%, H 9.93%, N 3.28%, P 3.63%. Found: C 59.26%, H 9.64%, N 3.43%, P 3.65%.

1-Stearoyl-2-{6-[α-methyl-4-(2-methylpropyl)benzeneacetamido]hexanoyl}-sn-glycero-3-phosphatidylcholine.



White wax. Hygroscopic. Yield 50%.

TLC analysis: One spot. R_f is 0.38.

^{1}H NMR (CD_3OD), δ (ppm): 0.88-0.93 (m, 9H), 1.29 (broad s, 31H), 1.40-1.48 (m+d, 6H), 1.55-1.62 (m, 4H), 1.78-1.90 (m, 1H), 2.27-2.35 (m, 4H), 2.43-2.46 (d, 2H), 3.11-3.16 (m, 2H), 3.22 (s, 9H), 3.56-3.66 (m, 3H), 4.00-4.03 (t, 2H), 4.18-4.28 (several m, 4H), 5.18 (m, 1H), 7.07-7.11 (d, 2H), 7.22-7.25 (d, 2H).

^{31}P NMR (CD_3OD), δ (ppm): -0.20(s).

Chemical analysis: $C_{45}H_{81}N_2O_9P$. $2.5H_2O$. Calculated: C 62.07%, H 9.89%, N 3.22%, P 3.56%. Found: C 62.00%, H 10.01%, N 3.32%, P 3.19%.

CN Bruflam
CN Brufort
CN Buburone
CN Buluofen
CN Burana
CN Butacortelone
CN Butylenin
CN Carol
CN **Ibuprofen**
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY
FS 3D CONCORD
DR 58560-75-1, 139466-08-3
MF C13 H18 O2
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DIPPR*, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IMSCOSEARCH, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PATDPASPC, PHAR, PIRA, PROMT, PROUSDDR, PS, RTECS*, SCISEARCH, SPECINFO, SYNTHLINE, TOXCENTER, ULIDAT, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**, WHO
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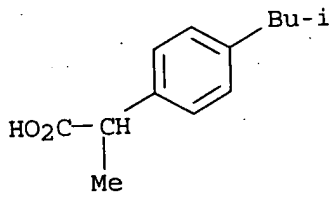

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

7974 REFERENCES IN FILE CA (1907 TO DATE)
236 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
7994 REFERENCES IN FILE CAPLUS (1907 TO DATE)
2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> s ketoprofen/cn
L7 1 KETOPROFEN/CN

=> d

L7 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2005 ACS on STN
RN 22071-15-4 REGISTRY
ED Entered STN: 16 Nov 1984
CN Benzeneacetic acid, 3-benzoyl-α-methyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Hydratropic acid, m-benzoyl- (8CI)
OTHER NAMES:
CN (±)-2-(3-Benzoylphenyl)propionic acid
CN (±)-3-Benzoyl-α-methylbenzeneacetic acid
CN (±)-Ketoprofen
CN (±)-m-Benzoylhydratropic acid
CN (RS)-Ketoprofen

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Bib Data Sheet

CONFIRMATION NO. 3472

SERIAL NUMBER	FILING DATE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
10/757,098	01/14/2004 RULE	514	1626	800.1012DIV

APPLICANTS

Alexander Kozak, Rehovot, ISRAEL;

Israel Shapiro, Ramla, ISRAEL;

** CONTINUING DATA **********

This application is a DIV of 09/856,009 05/16/2001 PAT 6,730,696 *
which is a 371 of PCT/IL99/00623 11/18/1999
(*)Data provided by applicant is not consistent with PTO records.

** FOREIGN APPLICATIONS **********

ISRAEL 127143 11/18/1998

Filed in 2/856,009 RK

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** 04/16/2004

Foreign Priority claimed	STATE OR	SHEETS	TOTAL	INDEPENDENT
35 USC 119 (a-d) conditions met	COUNTRY	DRAWING	CLAIMS	CLAIMS
Verified and Acknowledged	ISRAEL	4	33	3

☒ yes ☐ no

☒ yes ☐ no ☐ Met after Allowance

Examiner's Signature Initials

ADDRESS
23280
DAVIDSON, DAVIDSON & KAPPEL, LLC
485 SEVENTH AVENUE, 14TH FLOOR
NEW YORK , NY
10018

TITLE
Phospholipid derivatives of non-steroidal anti-inflammatory drugs

FILING FEE	FEES: Authority has been given in Paper	☐ All Fees ☐ 1.16 Fees (Filing) ☐ 1.17 Fees (Processing Ext. of

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Mary Hale, Information Branch Supervisor
Remsen Bldg. 01 D86
571-272-2507

Voluntary Results Feedback Form

- *I am an examiner in Workgroup:* ☐ *Example: 1610*
- *Relevant prior art **found**, search results used as follows:*
  - ☐ 102 rejection
  - ☐ 103 rejection
  - ☐ Cited as being of interest.
  - ☐ Helped examiner better understand the invention.
  - ☐ Helped examiner better understand the state of the art in their technology.

Types of relevant prior art found:

- ☐ Foreign Patent(s)
- ☐ Non-Patent Literature
  (journal articles, conference proceedings, new product announcements etc.)

- *Relevant prior art **not found**:*
  - ☐ Results verified the lack of relevant prior art (helped determine patentability).
  - ☐ Results were not useful in determining patentability or understanding the invention.

Comments:

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=> fil reg; d stat que l5; fil capl uspatf toxcenter; s l5; fil marpat; d stat que
l8
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STRUCTURE FILE UPDATES:    9 JAN 2006  HIGHEST RN 871542-42-6
DICTIONARY FILE UPDATES:   9 JAN 2006  HIGHEST RN 871542-42-6

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**********************************************************************
*                                                                    *
* The CA roles and document type information have been removed from *
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* effective March 20, 2005.  A new display format, IDERL, is now     *
* available and contains the CA role and document type information.  *
*                                                                    *
**********************************************************************

Structure search iteration limits have been increased.  See HELP SLIMITS
for details.

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L1                STR
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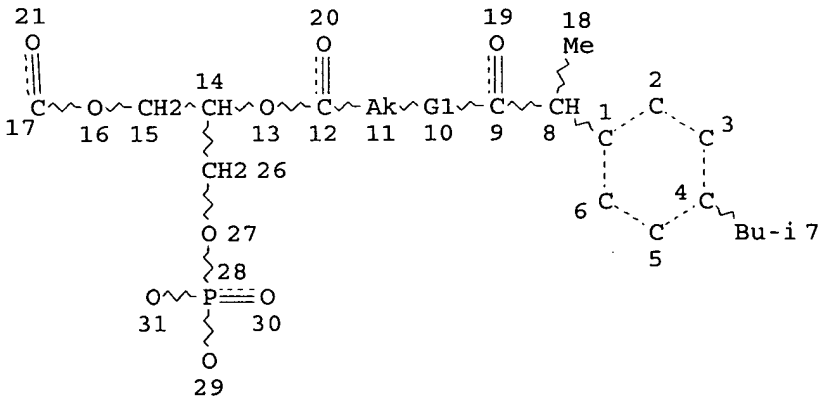


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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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NUMBER OF NODES IS 27

STEREO ATTRIBUTES: NONE
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FILE CONTENT: 1988-PRESENT (VOL 144 ISS 1 (20060101/ED)

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(COVERAGE TO THESE DATES IS NOT COMPLETE):

US 6949561 27 SEP 2005
DE 1020040544 15 SEP 2005
EP 1582199 05 OCT 2005
JP 2005320486 17 OCT 2005
WO 2005110983 24 NOV 2005

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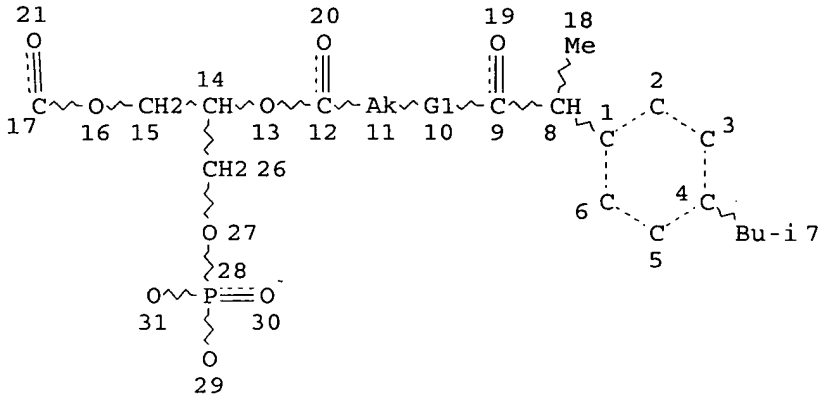
L6 STR



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MLEVEL IS CLASS AT 11
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NUMBER OF NODES IS 27

STEREO ATTRIBUTES: NONE
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PROCESSING COMPLETED FOR L8
L10 3 DUP REM L9 L8 (2 DUPLICATES REMOVED)
ANSWER '1' FROM FILE CAPLUS
ANSWERS '2-3' FROM FILE USPATFULL

— these are all the references to your compound - no sense in further narrowing with "method of using"

=> d ibib ed abs hitstr 1-3

L10 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 2000:368364 CAPLUS
DOCUMENT NUMBER: 133:12744
TITLE: Phospholipid derivatives of nonsteroidal antiinflammatory drugs
INVENTOR(S): Kozak, Alexander; Shapiro, Israel
PATENT ASSIGNEE(S): D-Pharm Ltd., Israel
SOURCE: PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000031083	A1	20000602	WO 1999-IL623	19991118
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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EP 1131326	A1	20010912	EP 1999-956297	19991118
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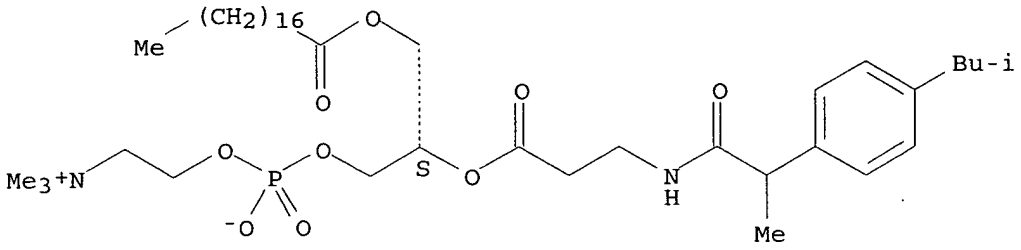
AU 766045	B2	20031009	AU 2000-12928	19991118
IL 142683	A1	20040620	IL 1999-142683	19991118
ZA 2001002718	A	20011005	ZA 2001-2718	20010403
US 6730696	B1	20040504	US 2001-856009	20010516
US 2004147485	A1	20040729	US 2004-757098	20040114

PRIORITY APPLN. INFO.:
IL 1998-127143 A 19981119
WO 1999-IL623 W 19991118
US 2001-856009 A3 20010516

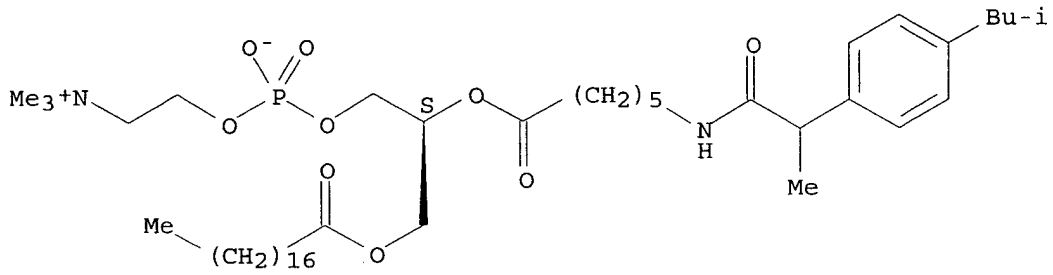
OTHER SOURCE(S): MARPAT 133:12744
ED Entered STN: 04 Jun 2000
AB The invention discloses compds. comprising nonsteroidal antiinflammatory drugs (NSAIDs) covalently linked to a phospholipid moiety via a bridging group. The invention further discloses a process for the synthesis of the compds., pharmaceutical compns. comprising them, and their use for the treatment of diseases and disorders related to inflammatory conditions.
IT **271781-47-6P 271781-48-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(NSAID-phospholipid conjugate preparation, pharmaceutical compns. and therapeutic use)
RN 271781-47-6 CAPLUS
CN β-Alanine, N-[2-[4-(2-methylpropyl)phenyl]-1-oxopropyl]-, (1S)-4-hydroxy-8,8-dimethyl-4-oxido-1-[[(1-oxooctadecyl)oxy]methyl]-3,5-dioxa-8-azonia-4-phosphanon-1-yl ester, inner salt, (7S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 271781-48-7 CAPLUS
CN 3,5,8-Trioxa-15-aza-4-phosphaoctadecan-1-aminium, 4-hydroxy-N,N,N-trimethyl-17-[4-(2-methylpropyl)phenyl]-9,16-dioxo-7-[[(1-oxooctadecyl)oxy]methyl]-, inner salt, 4-oxide, (7S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 2 OF 3 USPATFULL on STN
ACCESSION NUMBER: 2004:190712 USPATFULL
TITLE: Phospholipid derivatives of non-steroidal anti-inflammatory drugs
INVENTOR(S): Kozak, Alexander, Rehovot, ISRAEL
Shapiro, Israel, Ramla, ISRAEL
PATENT ASSIGNEE(S): D-Pharm, Ltd., Rehovot, ISRAEL (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004147485	A1	20040729
APPLICATION INFO.:	US 2004-757098	A1	20040114 (10)

RELATED APPLN. INFO.: Division of Ser. No. US 2001-856009, filed on 16 May 2001, GRANTED, Pat. No. US 6730696 A 371 of International Ser. No. WO 1999-IL623, filed on 18 Nov 1999, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	IL 1998-127143	19981118

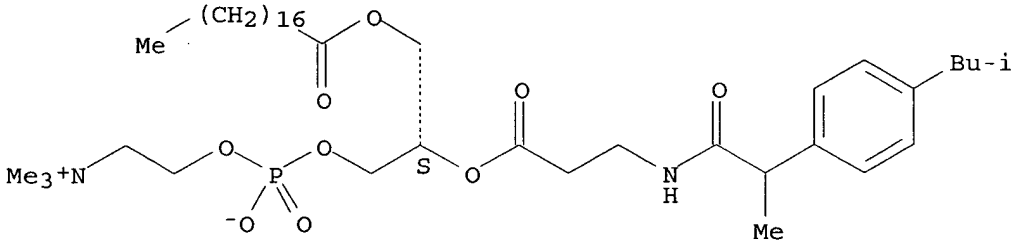
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: DAVIDSON, DAVIDSON & KAPPEL, LLC, 485 SEVENTH AVENUE,

14TH FLOOR, NEW YORK, NY, 10018
NUMBER OF CLAIMS: 33
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 4 Drawing Page(s)
LINE COUNT: 1858
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are compounds having non-steroidal anti-inflammatory drugs (NSAIDS) covalently linked to a phospholipid moiety via a bridging group. Also disclosed are a process for the synthesis of the compounds, pharmaceutical compositions comprising the compounds and the use thereof for the treatment of diseases and disorders related to inflammatory conditions, such as the treatment of ischemia.

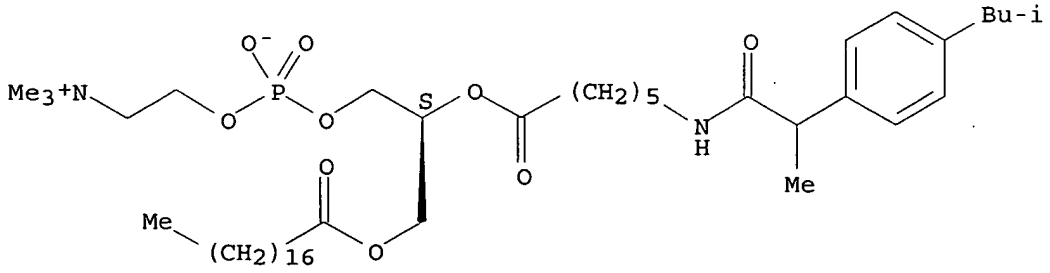
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **271781-47-6P 271781-48-7P**
(NSAID-phospholipid conjugate preparation, pharmaceutical compns. and therapeutic use)
RN 271781-47-6 USPATFULL
CN β-Alanine, N-[2-[4-(2-methylpropyl)phenyl]-1-oxopropyl]-, (1S)-4-hydroxy-8,8-dimethyl-4-oxido-1-[[(1-oxooctadecyl)oxy]methyl]-3,5-dioxa-8-azonia-4-phosphanon-1-yl ester, inner salt, (7S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 271781-48-7 USPATFULL
CN 3,5,8-Trioxa-15-aza-4-phosphaoctadecan-1-aminium, 4-hydroxy-N,N,N-trimethyl-17-[4-(2-methylpropyl)phenyl]-9,16-dioxo-7-[[(1-oxooctadecyl)oxy]methyl]-, inner salt, 4-oxide, (7S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L10 ANSWER 3 OF 3 USPATFULL on STN
ACCESSION NUMBER: 2004:109956 USPATFULL
TITLE: Phospholipid derivatives of non-steroidal

anti-inflammatory drugs
INVENTOR(S): Kozak, Alexander, Rehovot, ISRAEL
Shapiro, Israel, Ramla, ISRAEL
PATENT ASSIGNEE(S): D-Pharm, Ltd., Rehovot, ISRAEL (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6730696	B1	20040504	
	WO 2000031083		20000602	
APPLICATION INFO.:	US 2001-856009		20010516	(9)
	WO 1999-IL623		19991118	

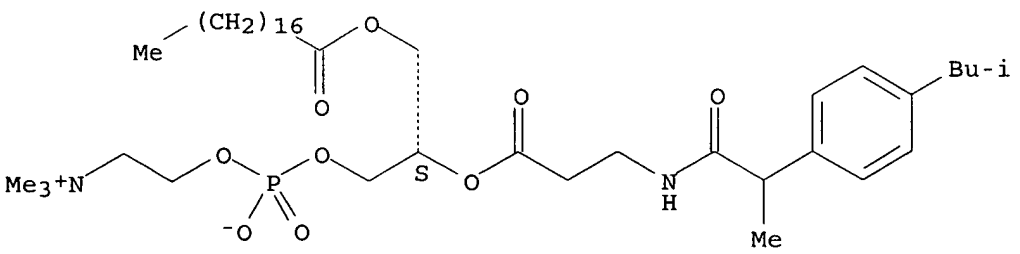
	NUMBER	DATE
PRIORITY INFORMATION:	IL 1998-127143	19981119

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: McKane, Joseph K.
ASSISTANT EXAMINER: Wright, Sonya
LEGAL REPRESENTATIVE: Davidson, Davidson & Kappel, LLC
NUMBER OF CLAIMS: 27
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 5 Drawing Figure(s); 4 Drawing Page(s)
LINE COUNT: 1796
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are compounds having non-steroidal anti-inflammatory drugs (NSAIDS) covalently linked to a phospholipid moiety via a bridging group. Also disclosed are a process for the synthesis of the compounds, pharmaceutical compositions comprising the compounds and the use thereof for the treatment of diseases and disorders related to inflammatory conditions, such as the treatment of ischemia.

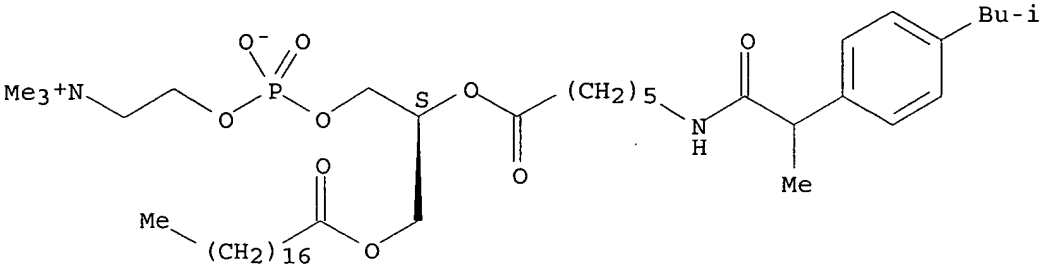
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **271781-47-6P 271781-48-7P**
(NSAID-phospholipid conjugate preparation, pharmaceutical compns. and therapeutic use)
RN 271781-47-6 USPATFULL
CN β-Alanine, N-[2-[4-(2-methylpropyl)phenyl]-1-oxopropyl]-, (1S)-4-hydroxy-8,8-dimethyl-4-oxido-1-[[(1-oxooctadecyl)oxy]methyl]-3,5-dioxa-8-azonia-4-phosphanon-1-yl ester, inner salt, (7S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 271781-48-7 USPATFULL
CN 3,5,8-Trioxa-15-aza-4-phosphaoctadecan-1-aminium, 4-hydroxy-N,N,N-trimethyl-17-[4-(2-methylpropyl)phenyl]-9,16-dioxo-7-[[(1-oxooctadecyl)oxy]methyl]-, inner salt, 4-oxide, (7S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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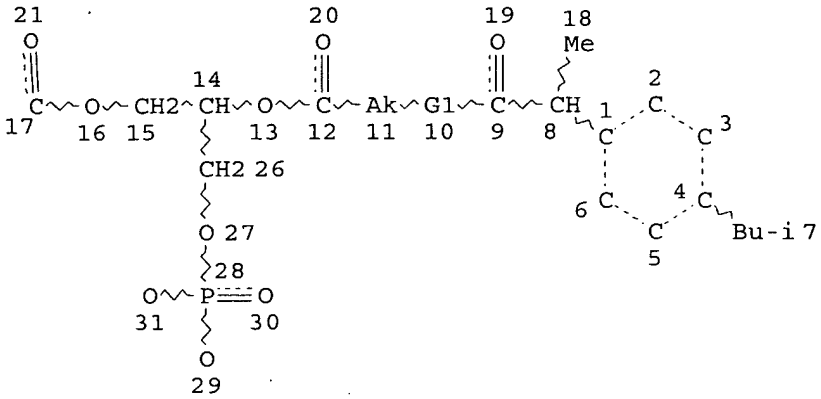

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MLEVEL IS CLASS AT 11
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 27

STEREO ATTRIBUTES: NONE
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SET LINE LOGIN
SET DETAIL LOGIN
D SCAN
SEL RN

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Searched by Barb O'Bryen, STIC 2-2518